| SEARCH REQUEST FORM |
|--|
| SEARCH REQUEST FORM Scientific and Technical Information Center |
| Requester's Full Name: Physical Number 30 & 47 03 Serial Number: 10 400 Date: 3129107 Art Unit: 1/6/4 Physical Number 30 & 47 03 Serial Number: 1/1/4502/1/28 26 Mail Box and Bldg/Room Location: 25 Results Format Preferred (circle): PAPER DISK E-MAIL 200 If more than one search is submitted, please prioritize searches in order of need. |
| Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract. |
| Title of Invention: Ey senol, alone or in combination with other yeart. |
| Inventors (please provide full names): |
| Earliest Priority Filing Date: 2/5/0/ |
| *For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number. |
| Earliest Priority Filing Date: & 15/0 *For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number. PUMUL AUN Ch: (PUMUL) (PUMUL |
| nomprining administrary ensural and, aptionally, applying |
| Point of Contact: Barb O'Bryen Technical Information Specialist STIC CM1 6A05 308-4291 |
| |

Access DB# 43

141711121

STAFF USE ONLY Vendors and cost where applicable Type of Search NA Sequence (#) STN Searcher: Searcher Phone #: AA Sequence (#)_ Questel/Orbit Structure (#) Searcher Location: Bibliographic Dr.Link_ Date Searcher Picked Up: 4-2-02 Date Completed: Litigation Lexis/Nexis Fulltext Searcher Prep & Review Time: ___ Sequence Systems Patent Family WWW/Internet Clerical Prep Time: Online Time: _

PTO-1590 (8-01)

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STRUCTURE FILE UPDATES: 31 MAR 2002 HIGHEST RN 403694-27-9 DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403694-27-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
L1
     97-53-0 REGISTRY
RN
     Phenol, 2-methoxy-4-(2-propenyl)- (9CI) (CA INDEX NAME)
CN
OTHER CA INDEX NAMES:
     Phenol, 4-allyl-2-methoxy- (8CI)
OTHER NAMES:
     1-Allyl-4-hydroxy-3-methoxybenzene
CN
     2-Hydroxy-5-allylanisole
CN
     2-Methoxy-1-hydroxy-4-allylbenzene
CN
     2-Methoxy-4-(2'-propenyl)phenol
CN
     2-Methoxy-4-(2-propenyl)phenol
CN
     2-Methoxy-4-allylphenol
CN
     3-(3-Methoxy-4-hydroxyphenyl)propene
CN
     3-(4-Hydroxy-3-methoxyphenyl)-1-propene
CN
     4-Allyl-1-hydroxy-2-methoxybenzene
CN
     4-Allyl-2-methoxyphenol
CN
CN
     4-Allylquaiacol
     4-Hydroxy-3-methoxyallylbenzene
CN
     Caryophyllic acid
CN
     Eugenic acid
CN
Eugenol
     p-Allylguaiacol
CN
     p-Eugenol
CN
 FS
     3D CONCORD
```

C10 H12 O2

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPATFULL, VTB (*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

$$CH_2-CH$$
 CH_2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4577 REFERENCES IN FILE CA (1967 TO DATE)

129 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

4589 REFERENCES IN FILE CAPLUS (1967 TO DATE)

19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d rn cn

L28 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 362-07-2 REGISTRY

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Estra-1,3,5(10)-triene-3,17.beta.-diol, 2-methoxy- (7CI, 8CI)

N Estradiol, 2-methoxy- (6CI)

OTHER NAMES:

CN 2-Hydroxyestradiol 2-methyl ether

CN 2-Methoxyestra-1,3,5(10)-triene-3,17.beta.-diol

CN <2-Methoxyestradiol

CN NSC 659853

=> fil medl; d que 15; d que 114; d que 116; d que 110; d que 112; s 110 or 112 ELLE MEDLINE' ENTERED AT 16:11:41 ON 02 APR 2002

FILE LAST UPDATED: 1 APR 2002 (20020401/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

| L2 L3 L4 | 761 SEA FILE=M 15200 SEA FILE=M 45211 SEA FILE=M 0 SEA FILE=M | MEDLINE ABB=ON | EUGENOL/CT PROSTATE/CT PROSTATIC DISEASES+NT/CT L2 AND (L3 OR L4) |
|---|--|---|--|
| L2 L13 <l14< td=""><td>761 SEA FILE=M 183 SEA FILE=M 0 SEA FILE=M</td><td>MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON</td><td>EUGENOL/CT METHOXYESTRADIOL L2 AND L13</td></l14<> | 761 SEA FILE=M 183 SEA FILE=M 0 SEA FILE=M | MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON | EUGENOL/CT METHOXYESTRADIOL L2 AND L13 |
| L2 L15 Œ16 | 761 SEA FILE=N 3361 SEA FILE=N | MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON | ESTRADIOL (L) AA/CT SWINGS |
| L2 L6 L7 L8 L9 L10 | 1357852 SEA FILE= 21 SEA FILE= 12 SEA FILE= 359 SEA FILE= | MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON | EUGENOL/CT C4./CT = Neoplasmo (includes precancerous conditions |
| L2 L9 L11 | 359 SEA FILE= 70596 SEA FILE= | MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON MEDLINE ABB=ON | EUGENOL/CT L2(L) (AD OR PK OR PD OR TU)/CT ANTINEOPLASTIC AGENTS/CT L9 AND L11 |

5 L10 OR L12

(T88

=> fil capl; d que 121; d que 126; d que 127; d que 130; d que 132; s 121 or 127 or 130

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FILE COVERS 1907 - 2 Apr 2002 VOL 136 ISS 14 FILE LAST UPDATED: 30 Mar 2002 (20020330/ED)

283 SEA FILE=CAPLUS ABB=ON

1 SEA FILE=CAPLUS ABB=ON L20 AND L24

L20 L24

L27

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and $1/\overline{23/02}$. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the ${
m H/Z/CA/CAplus}$ files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

| L1 L17 L18 L20 cL21 | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE# (1A) OIL OR (EUGENIC OR CARYOPHYLLIC) (W) ACID OR ALLYLGUAIACOL 21982 SEA FILE=CAPLUS ABB=ON PROSTAT?/OBI 665 SEA FILE=CAPLUS ABB=ON L17 (L) (BAC OR PAC OR THU OR DMA)/RL - Roles 2 SEA FILE=CAPLUS ABB=ON L18 AND L20 BAC - Biological Activity PAC - pharmacological activity THU - therapeutic use 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE# (1A) OIL OR TABLE TREGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE# (1A) OIL OR TOTAL TREGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE# (1A) OIL OR |
|---------------------------------|---|
| L1 L17 L20 L23 L26 | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE#(1A)OIL OR (EUGENIC OR CARYOPHYLLIC) (W)ACID OR ALLYLGUAIACOL 665 SEA FILE=CAPLUS ABB=ON L17(L) (BAC OR PAC OR THU OR DMA)/RL 1609 SEA FILE=CAPLUS ABB=ON PRECANCER? 0 SEA FILE=CAPLUS ABB=ON L20 AND L23 |
| L1 L17 L20 | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE#(1A)OIL OR (EUGENIC OR CARYOPHYLLIC)(W)ACID OR ALLYLGUAIACOL 665 SEA FILE=CAPLUS ABB=ON L17(L) (D)C OF TREE |

665 SEA FILE=CAPLUS ABB=ON L17(L)(BAC OR PAC OR THU OR DMA)/RL

(CANCER? OR NEOPLAS?) (L) PROPHYLA?/OBI

| L1 L17 L20 L28 L29 | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE#(1A)OIL OR (EUGENIC OR CARYOPHYLLIC) (W)ACID OR ALLYLGUAIACOL 665 SEA FILE=CAPLUS ABB=ON L17(L) (BAC OR PAC OR THU OR DMA)/RL 1 SEA FILE=REGISTRY ABB=ON 362-07-2 344 SEA FILE=CAPLUS ABB=ON L28 OR NSC 659853/OBI OR METHOXYESTRADI OL/OBI 1 SEA FILE=CAPLUS ABB=ON L20 AND L29 |
|---|---|
| L1 L17 L20 L22 L25 ,L32. | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 7256 SEA FILE=CAPLUS ABB=ON L1 OR EUGENOL OR CLOVE#(1A)OIL OR (EUGENIC OR CARYOPHYLLIC) (W)ACID OR ALLYLGUAIACOL 665 SEA FILE=CAPLUS ABB=ON L17(L) (BAC OR PAC OR THU OR DMA)/RL 126633 SEA FILE=CAPLUS ABB=ON ANTITUMOR AGENTS+OLD/CT 20 SEA FILE=CAPLUS ABB=ON L20 AND L22 6 SEA FILE=CAPLUS ABB=ON L25 AND (TUMOR OR ANTICARCINOGEN?)/TI |
| | 8 L21 OR L27 OR L30 OR L32 embase; d que l39; d que l40; d que l41; d que l44; d que l46; d que l48 HBASE' ENTERED AT 16:12:37 ON 02 APR 2002 HT (C) 2002 Elsevier Science B.V. All rights reserved. |
| | OVERS 1974 TO 28 Mar 2002 (20020328/ED) |
| | has been reloaded. Enter HELP RLOAD for details. |
| This fi | ile contains CAS Registry Numbers for easy and accurate noe identification. |
| L33 L34 L35 | 933 SEA FILE=EMBASE ABB=ON EUGENOL/CT 8387 SEA FILE=EMBASE ABB=ON PROSTATE+NT/CT 40803 SEA FILE=EMBASE ABB=ON PROSTATE DISEASE+NT/CT 0 SEA FILE=EMBASE ABB=ON L33 AND (L34 OR L35) |
| L28 L33 L38 L40 | 1 SEA FILE=REGISTRY ABB=ON 362-07-2 933 SEA FILE=EMBASE ABB=ON EUGENOL/CT 330 SEA FILE=EMBASE ABB=ON L28 OR NSC 659853 OR METHOXYESTRADIOL 0 SEA FILE=EMBASE ABB=ON L33 AND L38 |
| L33 L36 L41 | 933 SEA FILE=EMBASE ABB=ON EUGENOL/CT 3818 SEA FILE=EMBASE ABB=ON PRECANCER/CT 2 SEA FILE=EMBASE ABB=ON L33 AND L36 |
| L33 L37 L43 L44 | 933 SEA FILE=EMBASE ABB=ON EUGENOL/CT 1049087 SEA FILE=EMBASE ABB=ON L37(L) (PC OR DT)/CT - Subhading PC - prevention B control 7 SEA FILE=EMBASE ABB=ON L43 AND L33 PC - prevention B control DT - dive therapy |

| L33 L45 L 46 | 23730 | SEA | FILE=EMBASE FILE=EMBASE FILE=EMBASE | ABB=ON | EUGENOL/CT ANTINEOPLASTIC L33 AND L45 | ACTIVITY/CT |
|-------------------------------|-------|-----|---|--------|---|-------------|
| | | | | | | |

L33 933 SEA FILE=EMBASE ABB=ON EUGENOL/CT L47 10004 SEA FILE=EMBASE ABB=ON CANCER INHIBITION/CT L48 4 SEA FILE-EMBASE ABB-ON L33 AND L47

=> s 141 or 144 or 146 or 148 12 L41 OR L44 OR L46 OR L48

=> fil cancer; d que 151; d que 161; d que 163; s 151 or 161 FILE 'CANCERLIT' ENTERED AT 16:13:01 ON 02 APR 2002

FILE COVERS 1963 TO 14 Jun 2001 (20010614/ED)

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2000 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

| L49 L50 L51 | 30235 | SEA /CT | FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON | PROSTATE/CT OR PROSTATIC DISEASES+NT |
|--|----------------------------|--------------------------|---|---|
| L49 L52 L53 L59 L60 L61 | 963083 52517 17 6 | SEA SEA SEA SEA | FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON | C4./CT = ncoplasma ANTINEOPLASTIC AGENTS/CT L49(L)PD/CT PD = pharmacology L59/MA.J |
| L28 L49 L62 L63 | 38 94 | SEA SEA L | FILE=REGISTRY ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON FILE=CANCERLIT ABB=ON | EUGENOL/CT L28 OR NSC 659853 OR METHOXYESTRADIO |

L91 3 L51 OR L61

=> fil wpids; d que 168; d que 169; d que 173; s 168 or 169 or 173 FILE 'WPIDS' ENTERED AT 16:13:18 ON 02 APR 2002 COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE LAST UPDATED: 21 MAR 2002 <20020321/UP> MOST RECENT DERWENT UPDATE 200219 <200219/DW> DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001. (EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION

SEE HELP COST <<<

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>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY
    RESOURCE, PLEASE VISIT
         http://www.derwent.com/chemistryresource/index.html <<<
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>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

```
17 SEA FILE=WPIDS ABB=ON NSC 659853 OR METHOXYESTRADIOL OR
L64
                (METHOXY OR METH OXY) (W) (ESTRADIOL OR ESTRA(W) (DIOL OR DI OL))
            904 SEA FILE=WPIDS ABB=ON EUGENOL OR CLOVE#(1A)OIL OR ALLYLGUAIACO
L65
                L OR ALLYL GUAIACOL OR (EUGENIC OR CARYOPHYLLIC) (W) ACID
              1 SEA FILE-WPIDS ABB-ON L64 AND L65
I-68
```

904 SEA FILE=WPIDS ABB=ON EUGENOL OR CLOVE#(1A)OIL OR ALLYLGUAIACO L65 L OR ALLYL GUAIACOL OR (EUGENIC OR CARYOPHYLLIC) (W) ACID 6812 SEA FILE=WPIDS ABB=ON PROSTAT? L66 317 SEA FILE=WPIDS ABB=ON PRECANCER? L67 1 SEA FILE=WPIDS ABB=ON L65 AND (L66 OR L67) L69

904 SEA FILE=WPIDS ABB=ON EUGENOL OR CLOVE#(1A)OIL OR ALLYLGUAIACO L65 L OR ALLYL GUAIACOL OR (EUGENIC OR CARYOPHYLLIC) (W) ACID 28845 SEA FILE=WPIDS ABB=ON (CANCER? OR NEOPLAS? OR MALIGNAN? OR L72 TUMOR? OR TUMOUR?)/TI 9 SEA FILE-WPIDS ABB-ON L65 AND L72

10 L68 OR L69 OR L73 L92

L73

=> fil napra; d que 176; d que 187 FIRE NAPRALERT' ENTERED AT 16:13:32 ON 02 APR 2002 COPYRIGHT (C) 2002 Board of Trustees of the University of Illinois, University of Illinois at Chicago.

Some records in this file are extremely long when displayed in the ALL format. The CHC (Character Count) field can be used to estimate record length. Type HELP CONTENT at the next arrow prompt (=>) for data content and search strategy information.

FILE COVERS 1650 TO 11 MAR 2002 (20020311/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

| L1 L65 | 1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN 904 SEA FILE=WPIDS ABB=ON EUGENOL OR CLOVE#(1A)OIL OR ALLYLGUAIACO L OR ALLYL GUAIACOL OR (EUGENIC OR CARYOPHYLLIC) (W)ACID |
|--------------------|---|
| L74 | 1036 SEA FILE=NAPRALERT ABB=ON L65 OR L1 |
| L75 | 602 SEA FILE=NAPRALERT ABB=ON PROSTAT? |
| _€ I±7 6 | O SEA FILE=NAPRALERT ABB=ON L74 AND L75 |

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L1
              1 SEA FILE=REGISTRY ABB=ON EUGENOL/CN
L65
            904 SEA FILE=WPIDS ABB=ON EUGENOL OR CLOVE#(1A)OIL OR ALLYLGUAIACO
                L OR ALLYL GUAIACOL OR (EUGENIC OR CARYOPHYLLIC) (W) ACID
L74
           1036 SEA FILE=NAPRALERT ABB=ON L65 OR L1
L77
           6097 SEA FILE=NAPRALERT ABB=ON CANCER? OR NEOPLAS? OR MALIGNAN? OR
                TUMOR? OR TUMOUR? OR PRECANCER?
            658 SEA FILE=NAPRALERT ABB=ON CARCINOGENESIS INHIBITION/CC
L82
           5254 SEA FILE=NAPRALERT ABB=ON ANTITUMOR ACTIVITY/CC
L83
             99 SEA FILE=NAPRALERT ABB=ON TUMOR PROMOTION INHIBITION/CC
L84
              3 SEA FILE=NAPRALERT ABB=ON L77(P)L74(P)(L82 OR L83 OR L84)
Æ87
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=> dup rem 191,188,189,190,192,187 FILE 'CANCERLIT' ENTERED AT 16:13:58 ON 02 APR 2002

FILE 'MEDLINE' ENTERED AT 16:13:58 ON 02 APR 2002

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ANSWERS '1-3' FROM FILE CANCERLIT ANSWERS '4-6' FROM FILE MEDLINE ANSWERS '7-13' FROM FILE CAPLUS ANSWERS '14-23' FROM FILE EMBASE ANSWERS '24-32' FROM FILE WPIDS ANSWERS '33-35' FROM FILE NAPRALERT

=> d ibib ab 193 1-32; d qrd 193 33-35; fil hom

L93 ANSWER 1 OF 35 CANCERLIT DUPLICATE 2 ACCESSION NUMBER: 2000409441 CANCERLIT

DOCUMENT NUMBER:

20409441

TITLE:

Cytotoxicity and radical intensity of eugenol, isoeugenol

or related dimers.

Atsumi T; Fujisawa S; Satoh K; Sakagami H; Iwakura I; Ueha AUTHOR:

T; Sugita Y; Yokoe I

Department of Oral Physiology, Meikai University School of CORPORATE SOURCE:

Dentistry, Saitama, Japan.

SOURCE: ANTICANCER RESEARCH, (2000). Vol. 20, No. 4, pp. 2519-24.

Journal code: 59L. ISSN: 0250-7005.

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) FILE SEGMENT:

MEDL; L; Priority Journals; Cancer Journals

LANGUAGE: English

MEDLINE 20409441 OTHER SOURCE:

200010 ENTRY MONTH:

To investigate the possible link between radicals and cytotoxicity of eugenol-related compounds, dimer compounds were synthesized from eugenol (4-allyl-2-methoxyphenol) or isoeugenol (4-propenyl-2-methoxyphenol): bis-eugenol (3,3'-dimethoxy-5,5'-di-2-propenyl-1,1'-biphenyl-2,2'-diol); dehydrodiisoeugenol (2-(3-methoxy-4-hydroxyphenyl)-3-methyl-5-(1-propenyl)-7-methoxy-2,3- dihydrobenzofuran) and alpha-di-isoeugenol (r-1-ethyl-5-hydroxy-t-3-(4-hydroxy-3-methoxyphenyl)-6-methoxy-c-2methylindane). Both the cytotoxic activity and the DNA synthesis inhibitory activity of these compounds against a salivary gland tumor cell line (HSG) and normal human gingival fibroblast (HGF) were decreased in the order of: dehydrodiisoeugenol, alpha-di-isoeugenol > isoeugenol > eugenol > bis-eugenol. Electron spin resonance (ESR) spectroscopy showed that dehydrodiisoeugenol, alpha-di-isoeugenol and eugenol, but not isoeugenol and bis-eugenol, produced phenoxyl radicals under alkaline condition (pH > 9.5). However, benzyl radicals were produced during the dimerization of isoeugenol to dehydrodiisoeugenol. The radical intensity of alpha-di- and dehydrodiisoeugenol appeared at relatively later incubation time than eugenol, suggesting that their phenoxyl radical was more stable than that of eugenol. Such a phenoxyl radical is produced by scavenging free radicals, during the inhibition of lipid peroxidation. Higher cytotoxic activity of isoeugenol dimers was thought to be induced by interaction with cell membranes via the lipophilic radical. The present study supports the notion that relative cytotoxicity of chemicals can be evaluated by measuring the radical intensity using ESR.

DUPLICATE 3 L93 ANSWER 2 OF 35 CANCERLIT

96190854 CANCERLIT ACCESSION NUMBER:

DOCUMENT NUMBER: 96190854

Effect of eugenol on the genotoxicity of established TITLE:

mutagens in the liver.

Rompelberg C J; Evertz S J; Bruijntjes-Rozier G C; van den AUTHOR:

Heuvel P D; Verhagen H

TNO Nutrition and Food Research Institute, Zeist, The CORPORATE SOURCE:

Netherlands.

FOOD AND CHEMICAL TOXICOLOGY, (1996). Vol. 34, No. 1, pp. SOURCE:

33-42.

Journal code: F3U. ISSN: 0278-6915.

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

MEDL; L; Priority Journals; Cancer Journals FILE SEGMENT:

English LANGUAGE:

MEDLINE 96190854 OTHER SOURCE:

ENTRY MONTH: 199606

The influence of in vivo treatment with eugenol on established mutagens was studied to determine whether eugenol has antigenotoxic potential. The effects of eugenol in rats was investigated in the unscheduled DNA synthesis (UDS) assay with established mutagens and the Salmonella typhimurium mutagenicity assay. In addition, the effect of in vivo treatment with eugenol on benzo[a]pyrene (B[a]P)-induced genotoxicity in human hepatoma cell line Hep G2 was investigated in the single-cell gel electrophoresis assay. The mutagenicity of B[a]P in the S. typhimurium mutagenicity assay was lower in liver S-9 fractions from control rats. Incubation of liver S-9 fractions from eugenol-treated rats with dimethylbenzanthracene (DMBA) had no antimutagenic effect. Eugenol did not modify UDS activity in hepatocytes isolated from rats pretreated with eugenol orally after exposure of these cells in vitro to DMBA and aflatoxin B1. Four different treatment schemes of combinations of B[a] P_{γ} and eugenol were examined in Hep G2 cells: pre-treatment with eugenol; simultaneous treatment with eugenol and B[a]P; a combination of these (pretreatment/simultaneous treatment); and post-treatment with eugenol. An increase in the genotoxicity of B[a]P was found in Hep G2 cells. No effect of eugenol on the genotoxicity of B[a]P was found with the pre- and

post-treatments. It is concluded that the effect of eugenol on genotoxicity induced by established mutagens is not univocal; in vivo treatment of rats with eugenol resulted in a reduction of the mutagenicity of B[a]P in the S. typhimurium mutagenicity assay, while in the UDS assay no effect of eugenol was found. In vitro treatment of cultured cells with eugenol resulted in an increase in genotoxicity of B[a]P. These findings indicate that there is only limited support for the antigenotoxic potential of eugenol in vivo.

L93 ANSWER 3 OF 35 CANCERLIT

DUPLICATE 4

ACCESSION NUMBER:

95189236 CANCERLIT

DOCUMENT NUMBER:

95189236

TITLE:

Inhibition of tumour promotion in mice by eugenol.

AUTHOR:

Sukumaran K; Unnikrishnan M C; Kuttan R

CORPORATE SOURCE:

Amala Cancer Research Centre, Amala Nagar, Thrissur.

SOURCE:

INDIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, (1994). Vol. 38, No. 4, pp. 306-8.

DOCUMENT TYPE:

Journal code: GLD. ISSN: 0019-5499. Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT:

MEDL; L; Priority Journals

LANGUAGE:

English

OTHER SOURCE:

MEDLINE 95189236

ENTRY MONTH:

199505

Number of tumours (papillomas) produced by the application of 7,12-dimethyl benz (a) anthracene as initiator and croton oil promoter in mice were considerably inhibited (84%) by the prior application of eugenol. Moreover, there was considerable decrease in the number of tumour bearing animals and their onset. Eugenol inhibited superoxide formation and lipid peroxidation and the radical scavenging activity may be responsible for its chemopreventive action.

L93 ANSWER 4 OF 35 MEDLINE

ACCESSION NUMBER: 1999145494

MEDLINE

DOCUMENT NUMBER:

99145494 PubMed ID: 9990138

TITLE:

In vitro and in vivo effects of phenolic antioxidants

against cisplatin-induced nephrotoxicity.

AUTHOR:

SOURCE:

Rao M; Kumar M M; Rao M A

CORPORATE SOURCE:

Department of Pharmaceutical Chemistry, College of

Pharmaceutical Sciences, Kasturba Medical College, Manipal,

Karnataka, 576 119, India.. info@mahe.ernet.in

JOURNAL OF BIOCHEMISTRY, (1999 Feb) 125 (2) 383-90.

Journal code: HIF; 0376600. ISSN: 0021-924X.

PUB. COUNTRY:

Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199906

ENTRY DATE:

Entered STN: 19990628

Last Updated on STN: 19990628 Entered Medline: 19990615

We have investigated the effect of phenolic antioxidants on AΒ cisplatin-induced cytotoxicity in vero (African Green Monkey Kidney) cells and in rat renal cortical slices in vitro, and on cisplatin-induced nephrotoxicity in rats in vivo. Incubation of cisplatin with vero cells resulted in time- and concentration-dependent cytotoxicity, as characterized by decreased tryphan blue exclusion (TBE) and increased release of lactate dehydrogenase (LDH) into the medium. Cisplatin also caused reduction of glutathione (GSH) in a concentration-dependent manner. In the rat renal cortical slices model, incubation of cisplatin for 120 min caused an increase in malondialdehyde (MDA), a decrease in GSH and inhibited p-aminohippurate (PAH) uptake in a concentration-dependent manner. Among phenolic antioxidants, isoeugenol (IG) was found to be more active against cisplatin-induced cytotoxicity in vero cells as well as in

rat renal cortical slices than eugenol (EG) and dehydrozingerone (DZ). However none of the test compounds were able to arrest the reduction of the GSH content induced by cisplatin in either the vero cells or the renal cortical slice model. Administration of cisplatin (3 mg/kg) i.p. to rats resulted in significant reduction of body weight, and elevation of blood urea nitrogen (BUN) and serum creatinine. Treatment with IG 10 mg/kg i.p. 1 h before cisplatin resulted in partial but significant protection against the cisplatin-induced reduction of body weight, and elevation of BUN and serum creatinine, the protection being 34, 46, and 62%, respectively. EG and DZ (10 mg/kg, i.p.) were found to be inactive in vivo. Because IG is a potent free radical scavenger and protects against cisplatin-induced toxicitiy, the present results have many clinical implications in chemotherapy and thus warrants further investigation.

MEDLINE L93 ANSWER 5 OF 35

MEDLINE 95032291 ACCESSION NUMBER:

PubMed ID: 7945541 95032291 DOCUMENT NUMBER:

1'-Hydroxyeugenol- and coniferyl alcohol derivatives as TITLE: effective inhibitors of 5-lipoxygenase and Cu(2+)-mediated low density lipoprotein oxidation. Evidence for a dual

mechanism.

Deigner H P; Wolf G; Ohlenmacher U; Reichling J AUTHOR:

Pharmazeutisch-Chemisches Institut, Universitat Heidelberg, CORPORATE SOURCE:

Fed. Rep. of Germany.

ARZNEIMITTEL-FORSCHUNG, (1994 Aug) 44 (8) 956-61. SOURCE:

Journal code: 91U; 0372660. ISSN: 0004-4172.

GERMANY: Germany, Federal Republic of PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE)

English LANGUAGE:

Priority Journals FILE SEGMENT:

199411 ENTRY MONTH:

Entered STN: 19941222 ENTRY DATE:

Last Updated on STN: 19970203 Entered Medline: 19941117

1'-Hydroxyeugenol- and epoxy-Z-coniferyl alcohol esters from Coreopsis AΒ species as well as synthetic derivatives of these natural compounds were examined as lipoxygenase inhibitors and as LDL (low density lipoprotein) - stabilizing agents. Most of the compounds displayed inhibitory activity on the formation of leukotrienes (LTB4 and LTC4) in a cellular (RBL-1 cells) assay as well as in a cell-free 5-lipoxygenase assay at concentrations of 4-24 mumol/l. No effect of selected compounds was observed on mammalian lipoxygenases with other specificity (12- and 15-lipoxygenase). The more lipophilic derivatives also effectively reduced Cu(2+)-mediated oxidation of LDL. The findings are discussed on the base of structure-activity relationships.

MEDLINE L93 ANSWER 6 OF 35

90290336 MEDLINE ACCESSION NUMBER:

PubMed ID: 3274615 90290336 DOCUMENT NUMBER:

[Apicectomy and replantation. Report of a clinical case]. TITLE:

Apicectomia e reimpianto. Descrizione di un caso clinico. Floris N; Di Nunzio A; Pittau A; Floris S; Puddu G; Pes I

AUTHOR: ARCHIVIO STOMATOLOGICO, (1988 Oct) 29 (4) 783-94. SOURCE:

Journal code: 8HO; 0372454. ISSN: 0004-0320.

Italy PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE)

Italian LANGUAGE:

Dental Journals FILE SEGMENT:

199007 ENTRY MONTH:

Entered STN: 19900824 ENTRY DATE:

Last Updated on STN: 19900824 Entered Medline: 19900726

The AA. report a case treated with cyst-enucleation, apicaectomy and tooth AΒ

replantation and then prosthetic management, which they control for the last twenty years, and beyond initial expectations, they could establish an astonishing result indeed.

L93 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1 ACCESSION NUMBER: 2000:289765 CAPLUS

DOCUMENT NUMBER: 132:318019

TITLE: Phenol derivatives for inhibiting the proliferation of

tumor cells

INVENTOR(S): Bundschuh, Gerhard

PATENT ASSIGNEE(S): Meckel-Spenglersan G.m.b.H., Germany

SOURCE: Ger. Offen., 12 pp.

CODEN: GWXXBX

DOCUMENT TYPE: LANGUAGE:

Patent German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------------|----------|----------------------|----------------------|----------|
| DE 19954040 | A1 | 20000504 | DE 1999-19954040 | 19991029 |
| WO 2000025763 WO 2000025763 | A2 A3 | 20000511 20001109 | WO 1999-DE3524 | 19991029 |

W: JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:

DE 1998-19851706 A1 19981030

The invention provides a means of inhibiting the proliferation of tumor cells. The means of the invention uses phenol derivs., in particular thymol, eugenol, Hydroxybenzoic acid and/or derivs., as well as mixts. thereof. Lymphoma cells and Melanoma cells were used as test cells.

L93 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER:

1992:462500 CAPLUS

DOCUMENT NUMBER:

117:62500

TITLE: ·

Sesquiterpenes from clove (Eugenia caryophyllata) as

potential anticarcinogenic agents

AUTHOR(S): CORPORATE SOURCE: Zheng, Guo Qiang; Kenney, Patrick M.; Lam, Luke K. T.

LKT Lab. Inc., Minneapolis, MN, 55413, USA

SOURCE:

J. Nat. Prod. (1992), 55(7), 999-1003

CODEN: JNPRDF; ISSN: 0163-3864

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Bioassay-directed fractionation of clove terpenes from the plant E. caryophyllata has led to the isolation of the following five active known compds.: .beta.-caryophyllene, .beta.-caryophyllene oxide, .alpha.-humulene, .alpha.-humulene epoxide I, and eugenol. Their structures were detd. on the basis of spectral anal. (hreims, 1H and 13C NMR). These compds. showed significant activity as inducers of the detoxifying enzyme glutathione S-transferase in the mouse liver and small intestine. The ability of natural anticarcinogens to induce detoxifying enzymes has been found to correlate with their activity in the inhibition of chem. carcinogenesis. Thus, these sesquiterpenes show promise as potential anticarcinogenic agents.

L93 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

2002:51983 CAPLUS

TITLE:

136:79754

Use of eugenol, aflone, and in combination with other

chemopreventative agents as prophylaxis for

Searched by Barb O'Bryen, STIC 308-4291

cancers

INVENTOR(S):

Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William Biochemix, Inc/, USA

PATENT ASSIGNEE(S):

SOURCE:

U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S.

Ser. No. 527,283, abandoned.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. KIND DATE PATENT NO. _____ ______ US 2001-780269 20010209 US 2002006918 20020117 A1 US 2000-527283 B2 20000317

PRIORITY APPLN. INFO.: The use of eugenol, alone and in combination with 2-methoxyestradiol (2-ME) in the context of prostate cancer prophylaxis and treatment.

L93 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:14611 CAPLUS

DOCUMENT NUMBER:

136:63649

TITLE:

Screening of natural compounds for inhibitory activity

on metastatic properties of tumor cells and

the metastasis in mice

AUTHOR(S):

Ogasawara, Masaru; Matsubara, Toshiyuki; Suzuki,

Hideyo

CORPORATE SOURCE:

Toyama Prefect. Inst. Pharm. Res., Toyama, 939-0363,

Japan

SOURCE:

Toyama-ken Yakuji Kenkyusho Nenpo (2001), Volume Date

2000, 28, 1-8

CODEN: TYKNEU; ISSN: 1340-8011 Toyama-ken Yakuji Kenkyusho

DOCUMENT TYPE:

PUBLISHER:

Journal Japanese

LANGUAGE: We examd. the effects of 75 kinds of natural compds. on the in vitro migration, invasion, growth, and metastatic development of colon 26-L5 cells. Evodiamine showed the most potent and selective inhibitory activity on tumor cell migration with and IC50 value of 1.25 .mu.g/mL, which was about 20 times lower than that for tumor cell proliferation. the other hand, most of anti-cancer drugs tested had little effect on tumor cell migration. Evodiamine inhibited Matrigel invasion of tumor cells in a concn.-dependent manner, and achieved 70% inhibition at 10 .mu.g/mL. Treatment of tumor cells with evodiamine for over 48 h resulted in a concn. - and time-dependent growth inhibition. Pretreatment of tumor cells with 10 .mu.g/mL evodiamine before inoculation into mice caused 70% redn. in their lung metastasis formation. When evodiamine at 10 mg/kg was administered into mice from the 6th day after tumor inoculation, the no. of tumor nodules in lungs was decreased by 48% as compared to control. On the other hand, cisplatin, a potent anti-cancer drug, produced 58% redn. Evodiamine did not affect the body wt. of mice in the exptl. period, whereas cisplatin caused serious wt. loss. These results suggest that evodiamine may be regarded as a leading compd. for anti-metastatic agents acting through the inhibition of tumor cell migration.

L93 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1999:311102 CAPLUS

DOCUMENT NUMBER:

130:332910

TITLE:

Methods and compositions for regulation of 5-alpha

reductase activity

INVENTOR(S): PATENT ASSIGNEE(S): Liao, Shutsung; Hiipakka, Richard A. Arch Development Corporation, USA

SOURCE:

PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
PATENT NO.
                         KIND DATE
                                                   APPLICATION NO. DATE
                                 -----
                                                   -----
      WO 9922728
                          A1 19990514
                                                 WO 1998-US23041 19981030
           W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
          N. AL, AL, AL, AL, BA, BB, BB, BB, BI, CA, CH, CN, CO, CZ, BL, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM GA GN GN MI MI MD NE SN TD TG
                CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      AU 9912898
                           A1
                                 19990524
                                                   AU 1999-12898
                                                                       19981030
      EP 1027045
                           A1
                                 20000816
                                                  EP 1998-956358
                                                                       19981030
           R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, SE, PT, IE
PRIORITY APPLN. INFO.:
                                                US 1997-63770P P 19971031
                                                WO 1998-US23041 W 19981030
OTHER SOURCE(S):
                              MARPAT 130:332910
      Compds. that inhibit 5.alpha.-reductase are provided. The compds. are
      used to treat prostate cancer, breast cancer, obesity, skin disorders and
      baldness.
REFERENCE COUNT:
                              2
                                     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                     RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L93 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                              1997:272273 CAPLUS
DOCUMENT NUMBER:
                              126:324869
TITLE:
                             A modified and convenient method for assessing
                              tumor cell invasion and migration and its
                              application to screening for inhibitors
                             Saito, Ken-Ichi; Oku, Tohru; Ata, Naomi; Miyashiro,
AUTHOR(S):
                             Hirotsugu; Hattori, Masao; Saiki, Ikuo
                             Department of Pathogenic Biochemistry, Research
CORPORATE SOURCE:
                             Institute for Wakan-Yaku (Traditional Sino-Japanese
                             Medicines, Toyama Medical and Pharmaceutical
                             University, Toyama, 930-01, Japan
Biol. Pharm. Bull. (1997), 20(4), 345-348
SOURCE:
                             CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER:
                             Pharmaceutical Society of Japan
DOCUMENT TYPE:
                             Journal
LANGUAGE:
                             English
     In order to screen potent inhibitors of tumor invasion and metastasis, we
AΒ
     here devised a simple and reproducible in vitro assay for tumor invasion
     and migration. A conventional cell-counting assay using a Transwell
     chamber with a microporous membrane filter is troublesome and
     time-consuming, involving visually counting the cells under a microscope,
     and the invaded or migrated cells are sometimes distributed unevenly in
     predetd. fields on the lower surface of the filter. Therefore, it is
     difficult to evaluate the invasive and migratory abilities of tumor cells
     easily and quant. by the cell counting method. In the present study,
     crystal violet dye was used for staining the invaded cells and
     colorimetrically assessing the invasive ability per filter as an
     absorbance. In this crystal violet assay, tumor cell invasion into a
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reconstituted basement membrane Matrigel was proportional to both the cell

The results obtained by this dye-uptake method were highly consistent with those of a conventional cell-counting assay. Using this crystal violet assay, the anti-invasive effect of doxorubicin (DOX) was detected more easily and found to be highly proportional to that by the conventional cell-counting method. We therefore applied this convenient assay method to screen anti-invasive and anti-metastatic compds. As a

no. added into the chamber and the incubation period, and inversely proportional to the amt. of Matrigel barrier on the upper surface of result, caffeic acid was found to be more active in the inhibition of both tumor cell invasion and migration without showing direct cytotoxicity in vitro than other related compds.

L93 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2002 ACS

1994:671409 CAPLUS ACCESSION NUMBER:

121:271409 DOCUMENT NUMBER:

Studies on possible protective effect of plant derived TITLE:

phenols and the vitamin precursors, .beta.-carotene

and .alpha.-tocopherol, on 7,12

dimethylbenz(a)anthracene-induced tumor

initiation events

Moushumi, Lahiri; Bhide, Sumati V. AUTHOR(S):

C.U. Shah College Pharmacy, SNDT Women's University, CORPORATE SOURCE:

Bombay, 400 049, India

Phytother. Res. (1994), 8(4), 237-40 SOURCE:

CODEN: PHYREH; ISSN: 0951-418X

Journal DOCUMENT TYPE: English LANGUAGE:

Our earlier expts. have shown that the plant phenols, hydroxychavicol, eugenol, catechin, and curcumin, and the vitamins, .beta.-carotene and .alpha.-tocopherol, are potent inhibitors of polycyclic arom. hydrocarbon (PAH)-induced mutagenesis and carcinogenesis. In an attempt to elucidate their mode of action, we studied their effect on mouse skin DNA synthesis following 7,12 dimethylbenzanthracene (DMBA) treatment and 3H-7,12 dimethylbenzanthracene-DNA interaction in vitro (in the presence of mouse skin S9). With the exception of eugenol, all the phenols and vitamins tested inhibited 3H-DMBA-DNA interaction in vitro. In the DNA biosynthesis assay, of the chemopreventive agents tested only .beta.-carotene effectively modulated DMBA-suppressed DNA synthesis in the mouse skin. Our results indicate that the assay of DNA biosynthesis is not of predictive value with respect to the chemopreventive effect of a chem., while assay of carcinogen-DNA interaction shows correlation between the chemopreventive property and the inhibition of the interaction of carcinogen with DNA.

L93 ANSWER 14 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

2002001157 EMBASE

TITLE:

Volatile isoprenoid constituents of fruits, vegetables and herbs cumulatively suppress the proliferation of murine B16

melanoma and human HL-60 leukemia cells.

AUTHOR:

Tatman D.; Mo H.

CORPORATE SOURCE:

H. Mo, Department of Nutrition Science, Texas Woman's University, P.O. Box 425888, Denton, TX 76204, United

States. hmo@twu.edu

SOURCE:

Cancer Letters, (25 Jan 2002) 175/2 (129-139).

Refs: 44

ISSN: 0304-3835 CODEN: CALEDQ

PUBLISHER IDENT .:

s 0304-3835(01)00723-6

COUNTRY:

Ireland

DOCUMENT TYPE: FILE SEGMENT:

Journal; Article 016 Cancer 025 Hematology 030 Pharmacology

Drug Literature Index 037

LANGUAGE:

English

English SUMMARY LANGUAGE:

Substantial evidence from epidemiological studies supports the inverse association between the intake of fruits, vegetables and other plant products and cancer incidence. Cancer-preventive constituents of fruits and vegetables may inhibit carcinogen activation, enhance carcinogen detoxification, prevent carcinogens from interacting with critical target sites, or impede tumor progression. These activities, however, are

achievable only when levels of individual bioactive constituents reach beyond those attainable from a normal balanced diet. Isoprenoids, a broad class of mevalonate-derived phytochemicals ubiquitous in the plant kingdom, suppress the proliferation of tumor cells and the growth of implanted tumors. A search for volatile isoprenoid constituents of food products spanning seven plant families identified 179 isoprenoids. Of these, 41 purchased from commercial sources were screened for efficacy in suppressing the proliferation of murine B16 melanoma cells. Individual isoprenoids suppressed the proliferation of B16 and HL-60 promyelocytic leukemia cells with varying degrees of potency. Cell cycle arrest at the G(0)-G(1) phase and apoptosis account, at least in part, for the suppression. Blends of isoprenoids suppressed B16 and HL-60 cell proliferation with efficacies equal to the sum of the individual impacts. These findings suggest that the cancer-protective property of fruits, vegetables, and related products is partly conferred by the cumulative impact of volatile isoprenoid constituents. .COPYRGT. 2002 Elsevier Science Ireland Ltd. All rights reserved.

L93 ANSWER 15 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000210494 EMBASE

TITLE: Anethole blocks both early and late cellular responses

transduced by tumor necrosis factor: Effect on NF-.kappa.B,

AP-1, JNK, MAPKK and apoptosis.

AUTHOR: Chainy G.B.N.; Manna S.K.; Chaturvedi M.M.; Aggarwal B.B.

B.B. Aggarwal, Cytokine Research Laboratory, Department of CORPORATE SOURCE:

Bioimmunotherapy, Univ. TX M.D. Anderson Cancer Center,

Houston, TX 77030, United States

SOURCE: Oncogene, (8 Jun 2000) 19/25 (2943-2950).

Refs: 40

ISSN: 0950-9232 CODEN: ONCNES

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

Anethole, a chief constituent of anise, camphor, and fennel, has been shown to block both inflammation and carcinogenesis, but just how these effects are mediated is not known. One possibility is TNF-mediated signaling, which has also been associated with both inflammation and carcinogenesis. In the present report we show that anethole is a potent inhibitor of TNF-induced NF-.kappa.B activation (an early response) as monitored by electrophoretic mobility shift assay, I.kappa.B.alpha. phosphorylation and degradation, and NF-.kappa.B reporter gene expression. Suppression of I.kappa.-B.alpha. phosphorylation and NF-.kappa.B reporter gene expression induced by TRAF2 and NIK, suggests that anethole acts on I.kappa.B.alpha. kinase. Anethole also blocked the NF-.kappa.B activation induced by a variety of other inflammatory agents. Besides NF-.kappa.B, anethole also suppressed TNF-induced activation of the transcription factor AP-1, c-jun N-terminal kinase and MAPK-kinase. In addition, anethole abrogated TNF-induced apoptosis as measured by both caspase activation and cell viability. The anethole analogues eugenol and isoeugenol also blocked TNF signaling. Anethole suppressed TNF-induced both lipid peroxidation and ROI generation. Overall, our results demonstrate that anethole inhibits TNF-induced cellular responses, which may explain its role in suppression of inflammation and carcinogenesis.

L93 ANSWER 16 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999410171 EMBASE

TITLE: Enhancement in skin permeability of tamoxifen.

AUTHOR: Zhao K.; Singh J.

CORPORATE SOURCE: K. Zhao, College of Pharmacy, North Dakota State University, Fargo, ND 58105, United States

SOURCE: Proceedings of the Controlled Release Society, (1999) -/26

(186-187). Refs: 3

ISSN: 1022-0178 CODEN: 58GMAH

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer

027 Biophysics, Bioengineering and Medical

Instrumentation

030 Pharmacology

037 Drug Literature Index

039 Pharmacy

LANGUAGE: English

L93 ANSWER 17 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998412431 EMBASE

TITLE: Bioactive phytochemicals with emphasis on dietary

practices.

AUTHOR: Krishnaswamy K.; Raghuramulu N.

CORPORATE SOURCE: Dr. K. Krishnaswamy, National Institute of Nutrition,

Jamai-Osmania, Hyderabad 500007, India

SOURCE: Indian Journal of Medical Research, (1998) 108/NOV.

(167-181). Refs: 56

ISSN: 0971-5916 CODEN: IMIREV

COUNTRY: India

DOCUMENT TYPE: Journal; Article FILE SEGMENT: 016 Cancer

017 Public Health, Social Medicine and Epidemiology

029 Clinical Biochemistry 037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

Diet can modify the pathophysiological processes of various metabolic disorders and can be an effective preventive strategy for various disease processes most of which are known to involve oxidative damage. Both nutrient and non-nutrient components of the diet have been recognized for their anti-oxidant and other potential benefits. Plant foods contain phytochemicals such as flavonoids, phenolic acids, etc., which show biological activity. Some common foods used in Indian culinary practices were assessed for their anti-oxidant, anti-mutagenic and anti-carcinogenic effects and vitamin D activity and evaluated for their plausible biological effects. Green leafy vegetables had the highest anti-oxidant activity followed by wheat and rice. Cooking decreased this activity. Eugenol, the active principle of clove, was shown to offer protection against CCI4 induced hepatotoxicity in rats. It also showed anti-peroxidative activity in addition to decrease in O2 formation. Studies on the anti-carcinogenic effect of turmeric/curcumin revealed that both are potent anti-mutagens in vivo and reduce the adducted DNA levels in liver of rats challenged with B(a)P. In another study, Syrian hamsters receiving turmeric/curcumin through diet or local paint on cheek pouch had lower tumour burden as well as adducted DNA level against 7-12-DMBA challenge. Turmeric/curcumin were found to be better anti-tumour agents when given in the post initiation phase of carcinogenesis. The beneficial effect of turmeric was found to be due to its anti-oxidant potential. Studies on humans at risk of palatal cancer due to reverse smoking showed that turmeric (1 g/day) for 9 months had a significant impact on the regression of precancerous lesions. Onion and garlic also possess antimutagenic principle. Further studies on the bioactive phytochemicals in plants showed that certain plants belonging to Solanaceae (Cestrum diurnum, Lycopersicon esculentum and Solanum melongena) have calcinogenic potential and vitamin D like activity. In view of the vast data on

bioactive principles from plants, it is suggested that dietary prevention coupled with other life-style changes is perhaps the right answer for prevention of cancer and other chronic diseases in India.

L93 ANSWER 18 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

1998160291 EMBASE

TITLE:

Inhibition by eugenol of diethylnitrosamine-induced

microsomal degranulation. Selvi R.T.; Niranjali S.

AUTHOR: CORPORATE SOURCE:

R.T. Selvi, Department of Biochemistry, University of

Madras, Guindy Campus, Chennai - 600 025, India

SOURCE:

Fitoterapia, (1998) 69/2 (115-117). Refs: 20

ISSN: 0367-326X CODEN: FTRPAE

COUNTRY:

Italy

DOCUMENT TYPE: FILE SEGMENT:

Journal; Article 030 Pharmacology

037 Drug Literature Index

LANGUAGE:

English English

SUMMARY LANGUAGE:

The anticarcinogenic effect of eugenol (main component of clove oil) was detected by a simplified short-term technique based on the inhibition of microsomal degranulation of rat liver microsomes, in vitro. Our results suggest that eugenol protects the microsomes against the degranulatory attack by the carcinogen diethylnitrosamine.

ANSWER 19 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

97238760 EMBASE

DOCUMENT NUMBER:

1997238760

TITLE: AUTHOR: Natural origins of gynecologic treatment. Haefner H.K.; Pearce K.F.; Elkins T.E.

CORPORATE SOURCE:

Dr. H.K. Haefner, Dept. of Obstetrics and Gynecology, Univ. of Michigan Medical Center, MPB D 2202, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0718, United States

SOURCE:

Comprehensive Therapy, (1997) 23/7 (455-466).

Refs: 84

ISSN: 0098-8243 CODEN: COTHD3

COUNTRY:

United States

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT:

Obstetrics and Gynecology 010

030 Pharmacology

037 Drug Literature Index

LANGUAGE:

English

L93 ANSWER 20 OF 35 ACCESSION NUMBER:

COPYRIGHT 2002 ELSEVIER SCI. B.V. EMBASE

DOCUMENT NUMBER:

96065338 EMBASE

TITLE:

1996065338

AUTHOR .

Medium-term liver and multi-organ carcinogenesis bioassays

for carcinogens and chemopreventive agents.

CORPORATE SOURCE:

Ito N.; Hasegawa R.; Imaida K.; Hirose M.; Shirai T. Nagoya City Úniversity, 1 Kawasumi, Mizuho-cho, Mizuho-ku,

Nagoya 467, Japan

SOURCE:

Experimental and Toxicologic Pathology, (1996) 48/2-3

(113-119).

ISSN: 0940-2993 CODEN: ETPAEK

COUNTRY:

Germany

DOCUMENT TYPE:

Journal; Conference Article

FILE SEGMENT:

005 General Pathology and Pathological Anatomy

016 Cancer

052 Toxicology

037 Drug Literature Index

LANGUAGE:

English

SUMMARY LANGUAGE:

English

To bridge the gap between long-term carcinogenicity tests and short-term AΒ screening assays such as the Ames test, several types of medium-term bioassay for rapid detection of carcinogenic agents have been developed using male F344 rats. The liver model, in which diethylnitrosamine initiation and acceleration of carcinogenesis by partial hepatectomy are essential components, requires only 8 weeks of animal experimentation and a few weeks for quantitative analysis of hepatic preneoplastic lesions. Using the model, a total of 250 chemicals have been analyzed and the efficacy of the system for hapatocarcinogens has thereby been well established. Other models are so-called multi-organ bioassays for detection of carcinogenic agents in multiple several single organ carcinogenesis systems have demonstrated that carcinogenic and modifying effects of individual exogenous agents may markedly differ from organ to organ. Therefore, research into chemoprevention should be based on a whole body level analysis. The present mediumterm systems are very useful for this purpose.

L93 ANSWER 21 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

91150764 EMBASE

DOCUMENT NUMBER:

1991150764

TITLE:

Chemopreventive efficacy of betel leaf extract and its constituents on 7,12-dimethylbenz(a)anthracene induced carcinogenesis and their effect on drug detoxification

system in mouse skin.

AUTHOR:

Azuine M.A.; Amonkar A.J.; Bhide S.V.

CORPORATE SOURCE:

Carcinogenesis Division, Cancer Research Institute, Bombay

400 012, India

SOURCE:

Indian Journal of Experimental Biology, (1991) 29/4

(346-351).

ISSN: 0019-5189 CODEN: IJEBA6

COUNTRY:

India

DOCUMENT TYPE:

Journal; Article

FILE SEGMENT:

Dermatology and Venereology 013

Cancer 016

Clinical Biochemistry 029

Pharmacology 030

Drug Literature Index 037

LANGUAGE:

English

L93 ANSWER 22 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

CORPORATE SOURCE:

91009905 EMBASE

DOCUMENT NUMBER:

1991009905

TITLE:

Effects of naturally occurring antioxidants on combined 1,2-dimethylhydrazine- and 1-methyl-1-nitrosourea-initiated

carcinogenesis in F344 male rats.

AUTHOR:

Imaida K.; Hirose M.; Yamaguchi S.; Takahashi S.; Ito N. Department of Pathology, Nagoya City University Medical School, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467,

Japan

SOURCE:

Cancer Letters, (1990) 55/1 (53-59).

ISSN: 0304-3835 CODEN: CALEDQ

COUNTRY:

Ireland

DOCUMENT TYPE: FILE SEGMENT:

Journal; Article

Cancer 016

Gastroenterology 048

Toxicology 052 Drug Literature Index 037

English LANGUAGE:

SUMMARY LANGUAGE: English

The effects of treatment with naturally occurring antioxidants, selenium, .beta.-carotene, ferulic acid, esculin and eugenol during the promotional phase of tumor development were investigated in male F344 rats pre-treated with 1,2-dimethylhydrazine (DMH) and 1-methyl-1-nitrosourea (MNU). Animals

were given 3 subcutaneous injections of DMH at a dose of 40 mg/kg body wt. within 1 week and then were injected with MNU i.p. at a dose of 20 mg/kg body wt. 2 times per week, for 2 weeks. Thereafter, the rats were maintained on diet containing either 0.2% .beta.-carotene, 2 ppm selenium, 1% ferulic acid, 1% esculin or 0.8% eugenol. At week 52, surviving rats were killed and complete histological examinations were performed. Administration of eugenol enhanced the development of both hyperplasia and papillomas in the forestomach. Although treatment with .beta.-carotene tended to decrease the incidence and number of large intestinal carcinomas, .beta.-carotene, selenium, esculin and eugenol all decreased the incidence of kidney nephroblastomas, the differences were not statistically significant. The results thus showed that eugenol exerts promoting activity for forestomach carcinogenesis while the other antioxidants might have weak organ-specific inhibitory effects under these experimental conditions.

L93 ANSWER 23 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

87169773 EMBASE

DOCUMENT NUMBER:

1987169773

TITLE:

Induction of forestomach lesions in rats by oral

administrations of naturally occurring antioxidants for 4

AUTHOR:

Hirose M.; Masuda A.; Imaida K.; et al.

CORPORATE SOURCE:

First Department of Pathology, Nagoya City University

Medical School, Mizuho-ku, Nagoya 467, Japan

SOURCE:

Japanese Journal of Cancer Research, (1987) 78/4 (317-321).

CODEN: JJCREP

COUNTRY:

Japan Journal

DOCUMENT TYPE: FILE SEGMENT:

037 Drug Literature Index

016 Cancer

LANGUAGE:

English

The effects of naturally occurring antioxidants on rat forestomach epithelium were compared with those of synthetic antioxidants, butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), of which the former is a known forestomach carcinogen. Groups of five F344 male rats were given diet containing BHA, BHT, gallic acid, syringic acid, sesamol, caffeic acid, chlorogenic acid, ferulic acid, eugenol or esculin for 4 weeks at a level of 0.7% for BHT or 2% for other compounds. Histological examination of the forestomach showed that BHA induced hyperplasia mainly in the prefundic region near the esophageal orifice, caffeic acid induced pronounced hyperplasia throughout the forestomach epithelium, and sesamol induced large ulcers and hyperplasia in the central region. Thus, these naturally occurring antioxidants showed different toxicities and abilities to induce hyperplasia in the rat forestomach.

L93 ANSWER 24 OF 35 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER: DOC. NO. NON-CPI:

2001-6390**\$**6 [73] WPIDS N2001-477/709

DOC. NO. CPI:

TITLE:

C2001-18\$026

Use of 2-methoxyestradiol and its analogues for inhibit $\rlap{/}{z}$ ng proliferation and survival of pre-

cancerous and cancerous cells.

DERWENT CLASS: B01 P31

INVENTOR(S): PATENT ASSIGNEE(S): ALWORT, W; KUMAR, A P; SLAGA, T J; KUMAR, A; SLAGA, T (ONCO- \rlap/μ) ONCOLOGY SCI CORP; (BIOC-N) BIOCHEMIX INC

COUNTRY COUNT: PATENT INFORMATION:

> PATENT NO KIND DATE WEEK PG WO 2001070093 A2 20010927 (200173) * EN 37

83

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

Spivack

NL OA PT SD SE SL SZ TR /TZ UG ZW W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 2001047560 A 20011003 (200210) US 2002006918 A1 20020117 (20d212)

APPLICATION DETAILS:

| PATENT NO KIND | APPLICATION | DATE |
|--|---|--|
| WO 2001070093 A2 AU 2001047560 A US 2002006918 A1 CIP of | WO 2001-US8718 AU 2001-47560 US 2000-527283 US 2001-780269 | 20010319 20010319 20000317 20010209 |

FILING DETAILS:

| PATENT | NO | KIND | | | PAT | ENT | NO | _ |
|---------|--------|------|-------|----|-----|------|--------|---|
| | | | | | | | | • |
| AII 200 | 104756 | 60 A | Based | on | WO | 2001 | L70093 | |

20010209; US 2000-527283 PRIORITY APPLN. INFO: US 2001-780269 20000317; U\$ 2001-777151 20010205

WO 200170093 A UPAB: 2001121: NOVELTY - Inhibiting prolife‡ation and survival of pre-cancerous and cancerous cells involves administration of a composition containing 2methoxyestradiol to a cellular to a cellular aggregation.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition for application to cellular aggregation containing pre-cancerous or cancerous cells comprises at least one agent selected from 2-methoxyestradiol, 2-ethoxyestradiol, 2-butoxyestradiol, 17- alpha -ethynylestradiol with methoxy group at position 2, 17- alpha -ethynylestradiol with butoxy group at position 2, 17- alpha -ethynyl-9alpha -fluoroestradiol with methoxy group at position 2, or 17- alpha -ethynyl-9- alpha -fluoroestradiol with butoxy group at position 2.

ACTIVITY - Cytostatic MECHANISM OF ACTION - Cancerous cell growth inhibitor. The cells from androgen-dependent (LNCaP) and androgen-independent (DU145 and PC-3) cell lines were treated with different concentrations of 2methoxyestradiol (2-ME) (0.5 - 5 micro M) and cell growth, cell cycle progression and expression of p53 was monitored every 24 hours. Actively growing LNCaP and DU145 cells were plated in 96-well plates at a density of 105 cells per well. After 24 hours in a 37 deg. C incubator with 5 % CO2, the cells were treated. Control cells received only the vehicle dimethyl sulfoxide (DMSO) and cell growth was monitored every 24 hours using CELLTITER96 AQUEOUS ONE (solution assay containing a tetrazolium compound). The average of five replicates shows: control cells continued to proliferate during the time course while the cells treated with 2-ME showed a dose-dependent inhibition of cell proliferation. The androgen dependent LNCaP cell line was found more sensitive to the effect of 2-ME than the androgen independent DU145 cell line.

USE - For inhibiting proliferation and survival/for application to cellular aggregation pre cancerous and cancerous cells related to human prostrate cancer, human nervous system cancer, human skin cancer, brain cancer, lung cancer, colon cancer, pernicious mitosis of skin cells; for preventing onset of cancer or recurrence of cancer (all claimed).

ADVANTAGE - The composition is efficacious in inhibiting the proliferation and/or anglogenesis of cancer cells. The composition or it's analogs work synergistically with other compounds, notably eugenol to achieve even greater results and modality a 2-ME alone in attaching cancer cells (treatment of existing cancer), in preventing initial cancer

formation) or in preventing the recurrence of cancer. The use of 2-ME specifically targets (inhibits the growth) actively proliferating cells thus increasing its therapeutic index; the fact that 2-ME inhibits angiogenesis suggests that it can be used in the treatment of any type of cancer requiring the growth of blood vessels (angiogenesis); inhibits the growth of both androgen-dependent (LNCaP) and angrogen-independent (DU145) cells. Dwg.0/13

L93 ANSWER 25 OF 35 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:

2000-431201 [37] WPIDS

CROSS REFERENCE: DOC. NO. CPI:

2000-423217 [36]; 2000-442086 [36]

C2000-131000

TITLE:

Composition for preventing or treating soft tissue cancer comprises plant essential oil compound, e.g. benzyl alcohol, menthol or cinnamic alcohol, and a

transduction modulator.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BESSETTE, S M; ENAN, E E

PATENT ASSIGNEE(S):

(ECOS-N) ECOSMART TECHNOLOGIES INC

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT | ИО | KIND | DATE | WEEK | LA | PG |
|--------|----|------|------|------|----|----|
| | | | | | | |

WO 2000033858 AT 20000615 (200037) * EN 24

RW: AT BE CH GY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ

TM TR TT UA UG US UZ VN YU ZA ZW

AU 2000021671 A 20000626 (200045)

EP 1137427 A1 20011004 (200158) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

| PATENT NO KIND | APPLICATION | DATE |
|--|---|--|
| WO 2000033858 A1 AU 2000021671 A EP 1137427 A1 | WO 1999-US28889 AU 2000-21671 EP 1999-966021 WO 1999-US28889 | 19991207 19991207 19991207 19991207 |

FILING DETAILS:

| PA'] | PENT | NO | KIND | | PA1 | CENT N | 0 |
|----------|------|----------------------------|------|----------------|---------|--------|---|
| | | 00216 [.] 7427 | | Based Based | | 20003 | |

PRIORITY APPLN. INFO: US 1998-111271P 19981207

WO 200033858 A UPAB: 20011010 AΒ

NOVELTY - A pharmaceutical composition (I) for the prevention or treatment of soft tissue cancer in mammals comprises at least 1 plant essential oil compound and at least one signal transduction modulator.

ACTIVITY - Cytostatic; synergist.

MECHANISM OF ACTION - Antiestrogenic.

USE - (I) is used for the treatment and prevention of breast cancer (claimed).

Dwg.0/5

DERWENT INFORMATION LTD L93 ANSWER 26 OF 35 WPIDS COPYRIGHT 2002

2000-423217 [36] WPIDS ACCESSION NUMBER:

2000-431201 [36]; 2000-442086 [36] CROSS REFERENCE:

C2000-128078 DOC. NO. CPI:

Composition for preventing or treating soft tissue TITLE: cancer comprises plant essential oil compound

e.g. benzyl alcohol, menthol or cinnamic alcohol.

DERWENT CLASS: B04

BESSETTE, S M; ENAN, E E INVENTOR(S):

(ECOS-N) ECOSMART TECHNOLOGIES INC PATENT ASSIGNEE(S):

COUNTRY COUNT: 90

PATENT INFORMATION:

PG LAKIND DATE WEEK PATENT NO -----

WO 2000033857 Al 20000615 (200036)* EN 19 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ

TM TR TT UA UG US UZ VN YU ZA ZW

AU 2000021670 A 20000626 (200045) NO 2001002774 A. 20010606 (200154)

A1 20011004 (200158) EN EP 1137426

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CZ 2001001979 A3 20011017 (200172)

A 20011106 (200175) BR 9916879

KR 2001080692 A 20010822 (200213)

APPLICATION DETAILS:

| PATENT NO KI | ND | APPLICATION | DATE |
|---|----|---|--------------|
| WO 2000033857 AU 2000021670 NO 2001002774 | A | WO 1999-US288 AU 2000-21670 WO 1999-US288 NO 2001-2774 | 19991207 |
| EP 1137426 | A1 | EP 1999-96602 WO 1999-US28 | |
| CZ 2001001979 | А3 | WO 1999-US28 WO 1999-US28 CZ 2001-1979 | 888 19991207 |
| BR 9916879 | А | BR 1999-1687 WO 1999-US28 | 9 19991207 |
| KR 2001080692 | A | KR 2001-7070 | |

FILING DETAILS:

| PATENT NO K | IND | PATENT NO |
|--|-------------------------------------|--|
| AU 2000021670 EP 1137426 CZ 2001001979 BR 9916879 | Al Based on Al Based on Al Based on | WO 200033857 WO 200033857 WO 200033857 WO 200033857 |

PRIORITY APPLN. INFO: US 1998-111271P 19981207

WO 200033857 A UPAB: 20020226

NOVELTY - Composition (I) for the prevention or treatment of soft tissue cancer in mammals comprising at least 1 plant essential oil compound, is new.

ACTIVITY - Antiproliferative; Anti-estrogenic; Antimitogenic.

USE - (I) is used for the treatment and prevention of breast cancer. ADVANTAGE - The composition contains non-toxic materials thus leading to safer and more effective treatments for breast cancer. Dwg.0/0

L93 ANSWER 27 OF 35 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:

2000-442086 [38] WPIDS

CROSS REFERENCE:

2000-423217 [36]; 2000-431201 [36] C2000-134301

DOC. NO. CPI: TITLE:

Composition for preventing or treating soft tissue

cancer comprises plant essential oil compound,

e.g. benzyl alcohol, menthol or cinnamic alcohol, and a

transduction modulator.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BESSETTE, S M; ENAN, E E

PATENT ASSIGNEE(S):

(ECOS-N) ECOSMART TECHNOLOGIES INC

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LAPG

WO 2000033856 A1 20000615 (200038)* EN 32

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ

TM TR TT UA UG US UZ VN YU ZA ZW

AU 2000018419 A 20000626 (200045) EP 1137425 A1 20011004 (200158)

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

| PATENT NO KIND | APPLICATION | DATE |
|--|---|--|
| WO 2000033856 A1 AU 2000018419 A EP 1137425 A1 | WO 1999-US28766 AU 2000-18419 EP 1999-961937 WO 1999-US28766 | 19991207 19991207 19991207 19991207 |

FILING DETAILS:

| PATENT NO K | IND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000018419 | A Based on | WO 200033856 |
| EP 1137425 | Al Based on | WO 200033856 |

PRIORITY APPLN. INFO: US 1998-111271P 19981207

WO 200033856 A UPAB: 20011010

NOVELTY - A pharmaceutical composition (I) for the prevention or treatment of soft tissue cancer in mammals comprises at least 1 plant essential oil compound and at least one signal transduction modulator.

ACTIVITY - Cytostatic; synergist. MECHANISM OF ACTION - Antiestrogenic.

USE - (I) is used for the treatment and prevention of breast cancer. Dwg.0/9

L93 ANSWER 28 OF 35 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:

2000-640368 [62] WPIDS

DOC. NO. CPI:

C2000-192792

TITLE:

Antiseptic and analgesic composition, e.g. useful for

treating tumors and parodontal disease,

comprises Butamben and Eugenate.

DERWENT CLASS:

B05

INVENTOR(S):

SANGLIER TOUCHE, M J

PATENT ASSIGNEE(S):

(TOUC-I) SANGLIER TOUCHE M J

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|------------|------|----------|----------|-----|----|
| | | | | | |
| FR 2790389 | A1 | 20000908 | (200062) | k . | 7 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|------------|------|--------------|----------|
| | | | |
| FR 2790389 | A1 | FR 1999-2298 | 19990224 |

PRIORITY APPLN. INFO: FR 1999-2298 19990224

FR 2790389 A UPAB: 20001130

NOVELTY - Antiseptic and analgesic composition comprises Butamben (a local anesthetic comprising n-butyl p-aminobenzoate) and Eugenate (an antiseptic comprising zinc oxide and eugenol).

ACTIVITY - Analgesic; vulnerary; antimicrobial.

MECHANISM OF ACTION - None given.

USE - The composition is useful both for relieving acute or chronic pain, especially as a parodontal dressing or a post-operative surgical dressing for benign or malignant tumors or as a liquid for instillation into parodontal pouches or onto benign or malignant tumors, and for promoting wound healing and tissue repair.

ADVANTAGE - Combinations of Butamben and Eugenate have a synergistic effect with respect to pain relief, antisepsis, wound healing and tissue repair (no data given).

Dwq.0/0

DERWENT INFORMATION LTD L93 ANSWER 29 OF 35 WPIDS COPYRIGHT 2002

ACCESSION NUMBER:

WPIDS 1994-269372 [33] C1994-123143

DOC. NO. CPI: TITLE:

Anti-cancer agent - comprises substance having

super oxide dismutase activity.

DERWENT CLASS:

PATENT ASSIGNEE(S):

(KATO-I) KATO K; (NAKA-I) NAKANO M; (YUNI-N) YUNIE KK

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------|-----------|----------|-----------|----|----|
| JP 06199696 | - | 19940719 | (199433)* | | 5 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|---------------|----------|
| | | | |
| JP 06199696 | A | JP 1992-84860 | 19920306 |

PRIORITY APPLN. INFO: JP 1992-84860 19920306

JP 06199696 A UPAB: 19941010

New anti-cancer agent comprises the substance having superoxide dismutase (SOD) activity and/or anti-oxidative activity (including scavenger activity), phenol cpd. and sugar cpd. such as glycoprotein and saccharified flavonoid.

Phenol cpd. is pref. one substance selected from guaiacol, phenol, eugenol and phenyl ethanol, or a mixt. of those. Sugar cpd. is pref. one substance selected from asparatin, orientin (lutexin), cisorientin, isoquercetin and rutin or a mixt. of those.

USE/ADVANTAGE - The agent improves malignant tumour of mammals including human without causing side effects by being administered orally.

L93 ANSWER 30 OF 35 WPIDS COPYRIGHT 2002

WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:

1992-350977 [43] WPIDS

DOC. NO. CPI:

C1992-155747

TITLE:

Use of ether -type oil obtd. from cloves - for treatment

of benign prostate hyperplasia by oral or

rectal administration.

DERWENT CLASS:

B04

INVENTOR(S):

DEININGER, R

PATENT ASSIGNEE(S):

(CHIM-N) CHIMICASA GMBH

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------------------|------------|------------------------|-----------|----|----|
| EP 509268 R: AT CH | A1 DE E | 19921021 FR GB IT I | (199243)* | GE | 6 |
| DE 4112824 | | | | | 4 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|------------|------|-----------------|----------|
| EP 509268 | A1 | EP 1992-104865 | 19920320 |
| DE 4112824 | A | DE 1991-4112824 | |

PRIORITY APPLN. INFO: DE 1991-4112824 19910419

AB EP 509268 A UPAB: 19931115

Use of ethereal oil (clove oil) (I) isloated

from cloves (Flos Caryophylli; Syzygium aromaticum (L) Merrill et L.M.

Perry synonym: Engenia caryophyllata Thunberg), in treatment of

prostate hyperplasia by oral or anal intake, is new.

(I) is obtd. by steam distn. or extn. of whole or comminuted leaves, buds or stalks of clove plants. A compsn. contained engenol (80-90%, esp. 83%), acetylengenol (10-15%, esp. 11%) and alpha- and beta-caryolphyllene and caryophyllene oxide (5-12%, esp. 6%).

USE/ADVANTAGE - The product is natural and achieves a redn. in size of the **prostate**. The main component is engenol which is known as a spasmolytic agent. Admin. over a 12 month period is 100-1000 (esp. 250-400) mg/day (p.o.) or 200-2000 (esp. 400-800) mg/day anally for a 70 kg patient Dwg. 0/8

L93 ANSWER 31 OF 35 WPIDS COPYRIGHT 2002

WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER: DOC. NO. CPI:

1992-013071 [02] WPIDS

DOC. NO. CE

C1992-005761

TITLE:

Scavenger of active oxygen, esp. hydroxy radicals -

comprises coniferyl benzoate, eugenol, dehydro

di iso eugenol or iso-eugenol, used

for treating cancer, etc..

DERWENT CLASS:

B05 D21 E14

PATENT ASSIGNEE(S):

(KANE) KANEBO LTD

COUNTRY COUNT: `

1

PATENT INFORMATION:

PCT/US02/02826

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------------------|------|------|-----------------------|----|--------|
| JP 03263481 JP 2746453 | | | (199202)* (199823) | | 7 5 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|---------------|----------|
| JP 03263481 | A | JP 1990-61753 | 19900313 |
| JP 2746453 | B2 | JP 1990-61753 | 19900313 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO | | | | |
|------------|-----------------|-----------------|--|--|--|--|
| | | | | | | |
| JP 2746453 | B2 Previous Pub | ol. JP 03263481 | | | | |

PRIORITY APPLN. INFO: JP 1990-61753 19900313

JP 03263481 A UPAB: 19931006

Active O scavenger comprises coniferylbenzoate of formula (I), eugenol of formula (II), dehydrodiisoeugenol of formula (III) or

isoeugenol of formula (IV).

Coniferilbenzoate is obtd. from benzoate resin, eugenol is obtd. from clove or nutmeg oil by steam distn. dehydrodiisoeugenol is obtd. from nutmeg oil by steam distn. and isoeugenol is obtd. by heat isomerisation of eugenol with KOH in the presence of methanol or water.

USE/ADVANTAGE - It is used in medical applications and cosmetics. It effectively scavenges active O, esp. OH radicals which cause cancer and other diseases in human body. 0/0

L93 ANSWER 32 OF 35 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

ACCESSION NUMBER:

WPIDS 1991-337214 [46]

DOC. NO. CPI:

TITLE:

C1991-145694 New active oxygen scavengers of clove

oil or dehydro di eugenol - effective

against hydroxy radicals, used for treating inflammation,

cancer, ischaemic disorders, auto immune disease

etc..

DERWENT CLASS:

B05

(KANE) KANEBO LTD PATENT ASSIGNEE(S):

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------|------|----------|-----------|----|----|
| | | | | | |
| JP 03227938 | Α | 19911008 | (199146)* | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|---------------|----------|
| | | | |
| JP 03227938 | | JP 1990-22708 | 19900201 |

PRIORITY APPLN. INFO: JP 1990-22708 19900201 JP 03227938 A UPAB: 19930928

New active oxygen scavenger of formula (I) comprises clove oil or Dehydrodieugenol.

Clove oil is obtd. by purifying by vapour distillation of buds of Eugenia Caryophyllate. Dehydrodieugenol is prepd.

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by distillation of the purified oil of Eugenia Caryophyllate followed by
purificn. by silica gel chromatography.
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USE/ADVANTAGE - The scavenger is very effective against active oxygen esp. OH radical, which cause inflammation cancer, ischaemia disorder, radiation disorder, ageing, cataract and autoimmune disease. Dehydrodieugenol is safer and more practical than other scavengers because it does not have skin sensitisation activity. 0/0

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ANSWER 33 OF 35 NAPRALERT
 L93
                                  COPYRIGHT (C) 2002 BD. TRUSTEES, U. IL.
      92:59182 NAPRALERT
 ΑN
 DN
      M28085
      CHEMOPREVENTIVE EFFICACY OF BETEL LEAF EXTRACT AND ITS CONSTITUENTS ON
 TΤ
      7,12-DIMETHYLBEZ(A)ANTHRACENE INDUCED CARCINOGENSIS AND THEIR EFFECTON
      DRUG DETOXIFICATION SYSTEM IN MOUSE SKIN
 ΑU
      AZUINE M A; AMONKAR A J; BHIDE S V
     CARCINOGENSIS DIV, CANCER RESEARCH INST, BOMBAY 400 012 INDIA
 CS
 SO
     INDIAN J EXP BIOL (1991) 29 (4) p. 346-351.
 DT
      (Research paper)
LA
     ENGLISH
CHC
     4396
ORGN Class: DICOT Family: PIPERACEAE Genus: PIPER Species: BETLE
      Organism part: DRIED LEAF
      Geographic area (GT): INDIA; SAS
      TYPE OF STUDY (STY): IN VIVO. Classification (CC): CARCINOGENESIS
          INHIBITION
          Dosage Information: EXTERNAL; MOUSE; DOSE: 1.0 MG
          Qualitative results: ACTIVE
          Comment(s): VS.CARCINOGENESIS INDUCED BY 7,12-
                       DIMETHYLBENZ (A) ANTHRACENE..
                      MICE RECEIVED TREATMENT 2 WEEKS PRIOR TO CARCINOGEN
                      TREATMENT AND IMMEDIATELY THEREAFTER, 5 DAYS PER WEEK,
                       FOR 24 WEEKS. TUMOROGENESIS WAS INHIBITED BY
                       39%..
          COMPOUND. Chemical name (CN): EUGENOL
               Class identifier (CI): LIGNAN
L93
     ANSWER 34 OF 35 NAPRALERT
                                 COPYRIGHT (C) 2002 BD. TRUSTEES, U. IL.
ΑN
     92:55909 NAPRALERT
DN
     M24773
     EFFECT OF CHEMICAL CONSTITUENTS FROM PLANTS ON 12-O-TETRADECANOYLPHORBOL-
TI
     13-ACETATE-INDUCED INFLAMMATION IN MICE
ΑU
     YASUKAWA K; TAKIDO M; TAKEUCHI M; NAKAGAWA S
CS
     DEPT PHARM, COLL SCI & TECHNOL, NIHON UNIV, TOKYO 101 JAPAN
SO
     CHEM PHARM BULL (1989) 37 (4) p. 1071-1073.
DT
     (Research paper)
     ENGLISH
LA
CHC 28872
ORGN Class: DICOT
      TYPE OF STUDY (STY): IN VIVO. Classification (CC): TUMOR PROMOTION
          INHIBITION
          Dosage Information: EXTERNAL; MOUSE; DOSE: 2.0 MG per EAR
          Qualitative results: WEAK ACTIVITY
          Comment(s): VS.TPA-INDUCED EDEMA..
          COMPOUND. Chemical name (CN): EUGENOL
               Class identifier (CI): LIGNAN
```

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L93

ΑN DN 92:3350 NAPRALERT

A03698

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PHYTOCHEMISTRY OF THE BURSERACEAE
TI
     PERNET R
ΑU
     51 RUE AUDENET, PIERREFITTE 93 FRANCE
CS
     LLOYDIA (1972) 35 (3) p. 280-287.
SO
     (Research paper)
DT
LA
     FRENCH
CHC 13820
ORGN Class: DICOT Family: BURSERACEAE Genus: COMMIPHORA Species: ABYSSINICA
      Common name(s): MYRRH
      Organism part: GUM
      Geographic area (GT): ETHIOPIA; AFN
      TYPE OF STUDY (STY): FOLKLORE. Classification (CC): ANTITUMOR
          ACTIVITY
          Extract type: TYPE EXT NOT STATED
          Dosage Information: EXTERNAL; HUMAN ADULT
          Comment(s): USED AGAINST TUMORS.
          COMPOUND. Chemical name (CN): EUGENOL
               CAS Registry Number (RN): 97-53-0
               Class identifier (CI): LIGNAN
          COMPOUND. Chemical name (CN): SITOSTEROL, BETA
                CAS Registry Number (RN): 83-46-5
                Class identifier (CI): STEROID
          COMPOUND. Chemical name (CN): CAMPESTEROL
                CAS Registry Number (RN): 474-62-4
                Class identifier (CI): STEROID
           COMPOUND. Chemical name (CN): CHOLESTEROL
                CAS Registry Number (RN): 57-88-5
                Class identifier (CI): STEROID
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